PATENT
Attorney Docket No.: 019957-011210US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Examiner: Manjunath Rao
Paulson *et al.*	Art Unit: 1652
Application No.: 09/007,741	Declaration
Filed: January 15, 1998	
For: PRACTICAL IN VITRO SIALYLATION OF RECOMBINANT GLYCOPROTEINS	

Assistant Commissioner of Patents and Trademarks
Washington, D.C. 20231

Declaration Pursuant to 37 C.F.R. 1.132

Sir:

I, James C. Paulson, Ph.D., declare as follows:

I received an A.B. in chemistry and biology in 1970 from MacMurray College. I received an M.S. in Biochemistry in 1971 and a Ph.D. in Biochemistry in 1974, both from the University of Illinois at Champaign-Urbana. I was a postdoctoral fellow in the Department of Biochemistry at Duke University Medical Center in Durham, N.C. from 1974-1978. From 1978 to 1990 I was a faculty member in the Department of Biological Chemistry at the UCLA School of Medicine in Los Angeles, California including Assistant Professor (1978-1981), Associate Professor (1981-1985) and Professor and Vice-Chair (1985-1990). From 1990 to 1999 I was employed at Cytel Corporation in San Diego, California first as Vice President of Research and Development (1990-1996) and then Vice President, Chief Scientific Officer and General Manager of Glytec, a division of Cytel (1996-1999). Since 1999 I have been a Professor in the Department of Molecular Biology at the Scripps Research Institute in La Jolla, California.

EXHIBIT A

I have reviewed the above-referenced patent application and also the pending Office Action and references cited against the patent application. The method presently claimed features methods for sialylating a saccharide group on a recombinant glycoprotein that provide higher sialylation rates using lower sialyltransferase concentrations than are taught or suggested by the prior art.

I have reviewed Williams *et al.*, *Glycoconjugate J.* 12:755-761 (1995). Williams *et al.* do not disclose an identical method of sialylation of a glycoprotein as claimed in the above-referenced patent application. Williams *et al.* only disclose some recombinant sialyltransferases. Williams *et al.* do not quantitate the extent of sialylation of glycoprotein acceptors and certainly do not quantitate that at least 80-90% of the terminal saccharide is sialylated. Moreover, Williams *et al.* do not teach or suggest a sialyltransferase concentration of less than about 50 mU per mg of glycoprotein.

The experiments performed and reported by Williams *et al.* are designed to determine the K_M values of the sialyltransferases tested. In performing such experiments, it is necessary to maintain less than 20% saturation of substrate, i.e. terminal saccharide, in order to obtain valid kinetics allowing the K_M to be determined. In fact, when conducting such experiments, we specifically monitor to insure that we do not exceed 20% saturation of any substrate. Hence, Williams *et al.* cannot teach or suggest at least 80-90% of the terminal saccharide is sialylated.

I have reviewed the other three references cited by the Examiner, namely Wong *et al.*, U.S. Patent 5,374,541, Tsuiji *et al.*, *Glycobiology* 6:v-xiv (1996) and Paulson *et al.* U.S. Patent 5,541,083. None of these references teach or suggest methods wherein at least 80-90% of the terminal saccharide is sialylated. Moreover, none of the secondary references teach or suggest a sialyltransferase concentration of less than about 50 mU per mg of glycoprotein.

I further declare that all statements made in this Declaration of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Dated: 12/21/00 By _____

James C. Paulson, Ph.D.

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